A simple, cost-effective molecular assay may help manage growing spread of drug-resistant gonorrhea

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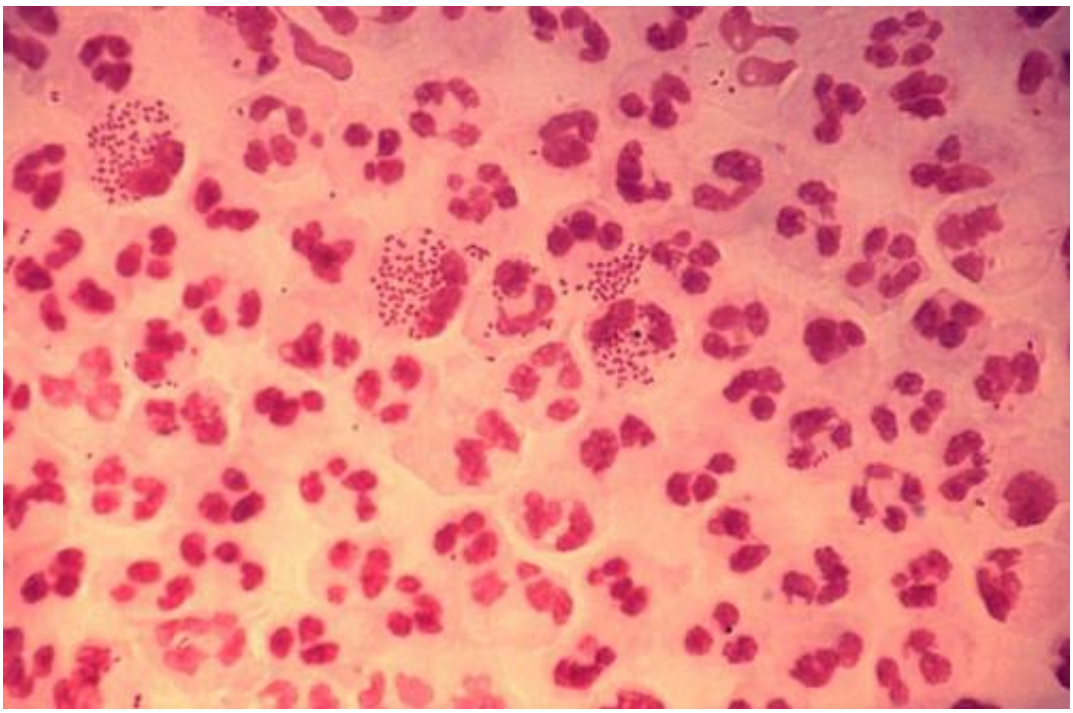

Credit: CDC

A dual therapy treatment regimen of expanded-spectrum cephalosporins (ESCs) plus azithromycin (AZM) is the recommended standard of care for gonorrhea. A strain of the Neisseria (N.) gonorrhoeae that is resistant to the ESC and AZM combination has emerged around the world with the potential to make gonorrhea untreatable. The currently used

screening methods for antimicrobial resistant (AMR) determinants are slow, expensive, and not widely available. In an article in *The Journal of Molecular Diagnostics*, published by Elsevier, researchers report a rapid and cheap method that can provide real-time surveillance to help control the spread of AMR strains of N. gonorrhoeae.

"N. gonorrhoeae has developed resistance to almost all classes of antibiotics that were previously recommended for treatment," explained lead investigator Junping Peng, MD, NHC Key Laboratory of Systems Biology of Pathogens, Institute of Pathogen Biology, and Key Laboratory of Respiratory Disease Pathogenomics, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China. "Timely determination and monitoring of AMR profiles are crucial for appropriately personalized treatment and maintenance of treatment effectiveness."

Current surveillance systems primarily depend on culture-based methods, which have high sensitivity but long turnaround times. Several nucleic acid amplification testing methods have been developed, but they are expensive and not widely available. Dr. Peng and his team have spent the past several years assessing the status of gonococcal AMR and the development of AMR screening technologies. They designed and developed a multiplex assay based on high-resolution melting (HRM) technology. Compared with other molecular methods that detect a single genetic mutation, HRM technology can detect the most frequent mutations associated with ESCs and AZM resistance in a single test. It uses a real time PCR system, equipment commonly found in most microbiological laboratories and clinical settings.

Forty-eight well-characterized N.gonorrhoeae clinical specimens and 15 non-gonococcal strains were selected for the initial assay establishment. The multiplex HRM assays were able to accurately identify different nucleotide variations of the AMR determinants related to ceftriaxone

and azithromycin resistance. Then, results from 556 multiplex HRM tests of clinical isolates and samples were compared with results from whole gene sequencing and PCR sequencing of the same samples. Compared with whole genome sequencing, the sensitivity, specificity, positive predictive value, and negative predictive value of the multiplex HRM assays for detection of AMR determinants were 98.6 percent, 99.2 percent, 98.6 percent, and 99.2 precent, respectively. The results were available within 90 minutes at a cost of less than $1.00 per sample.

This sequencing-free HRM assay may be applied to large-scale epidemiological programs for increasing surveillance of ESCs and AZM resistance and supporting identification and investigation of antimicrobial-resistant N. gonorrhoeae outbreaks in real-time. By application of this assay, gonococcal AMR surveillance could be enhanced significantly, resulting in improved management programs aimed at controlling the further spread of antimicrobial-resistant N. gonorrhoeae strains and pathogen eradication.

"Our team has been committed to the assessment of the current status of gonococcal AMR and the development of AMR screening technologies to provide scientific and technological support for the effective prevention and treatment of gonorrhea," observed Dr. Peng. This fast, simple, and cheap method could have significant implications in resource-limited countries with a high burden of disease."

More information: Leshan Xiu et al, Multiplex High-Resolution Melting Assay for Simultaneous Identification of Molecular Markers Associated with Extended-Spectrum Cephalosporins and Azithromycin Resistance in Neisseria gonorrhoeae, *The Journal of Molecular Diagnostics* (2020). DOI: 10.1016/j.jmoldx.2020.08.003